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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/625,963	07/26/2000	Hans Josef Stauss	ICI 101	8595

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PATREA L. PABST
PABST PATENT GROUP LLP
400 COLONY SQUARE
SUITE 1200
ATLANTA, GA 30361

EXAMINER	
VANDERVEGT, FRANCOIS P	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 09/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/625,963	STAUSS ET AL.	
	Examiner	Art Unit	
	F. Pierre VanderVegt	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5,7,15 and 19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5,7,15 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

5-00.

DETAILED ACTION

This application is a continuation of Application Serial Number PCT/GB99/03572.

Claims 2-4, 6, 8-14, 16-18, 20-48 have been canceled.

Claims 1, 5, 7, 15 and 19 are currently pending and are the subject of examination in the present Office Action.

In view of Applicant's amendment filed May 2, 2005 only the following ground of rejection is maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

1. Claims 1, 5, 7, 15 and 19 stand rejected under 35 U.S.C. 102(e) as being anticipated by the U.S. Patent Application Publication 20030082196 A1 (published May 1, 2003; on form PTO-892, of record), which claims priority to U.S. Patent Application serial number 09/164,223; filed September 30, 1998.

It was previously stated: "The '196 publication teaches the RMFPNAPYL peptide of instant SEQ ID NO: 1 as an immunogenic fragment of the human WT1 polypeptide as SEQ ID NO: 185 and as a fragment of the murine WT1 polypeptide as SEQ ID NO: 293 (paragraph 0008 and claim 5 in particular). The '196 publication teaches that immunogenic peptides of WT1 can be formulated into a pharmaceutical composition or vaccine (paragraphs 0109-0111 in particular) that can be used to "prevent, delay or treat a disease associated with WT1 expression" (paragraph 0120 in particular). The aforementioned teachings are disclosed in the parent 09/164,223) application. Applicant should note that, while the front page of the '196 publication does not refer to the relationship to the '223 application, the first paragraph of the specification does properly claim priority to the '233 application in the first paragraph. The prior art teaching anticipates the claimed invention.

Applicant's arguments filed July 30, 2004 have been fully considered but they are not persuasive. Applicant contends that the '196 does not anticipate the claimed peptides, pharmaceutical composition and vaccine because the '196 does not teach that "the peptide is processed by HLA-A0201-positive antigen presenting cells" and the reference therefore does not teach every element of the claim as required by the statute. However, Applicant's asserted limitation merely constitutes a manner for obtaining the peptide, thereby claiming the peptide in a product-by-process fashion, relying upon an intracellular processing step to distinguish the final product. The patentability of a product-by-process claim is

determined by the novelty and nonobviousness of the claimed product itself without consideration of the process for making it which is recited in the claim (see *In re* Thorpe, 227 USPQ 964 (Fed. Cir. 1985))." In the present case, the exact peptide, RMFPNAPYL, is taught by the '196 publication as an immunogenic fragment of WT1 and is the same as the instantly claimed peptide, irrespective of the manner of isolation or processing."

Applicant's arguments filed May 2, 2005 have been fully considered but they are not persuasive.

The declaration filed on May 2, 2005 under 37 CFR 1.131 has been considered but is ineffective to overcome the reference.

The declaration of co-inventors Stauss and Gao is defective because it does not identify where the claimed invention was reduced to practice. Paragraph 3 of the declaration identifies only that the attached pages "from our laboratory notebooks" demonstrated the reduction to practice. Paragraph 5 of the declaration states only that the reduction to practice took place before September 30, 1998. However, in order to be effective, the declaration must indicate that the reduction to practice took place in the United States or in a country having membership in the World Trade Organization on a date prior to the priority date of the published U.S. Patent application that Applicant is attempting to antedate. While it is noted that both inventors are residents of the United Kingdom, which was a WTO member prior to September 30, 1998, the reduction to practice may have taken place in a non-member nation. Accordingly, the ground of rejection is maintained for the reason of record, but may be overcome by the filing of a new affidavit under 37 CFR § 1.131 identifying the national location of the reduction to practice.

Furthermore, it is not readily apparent that the notebook pages submitted as part of the affidavit demonstrate possession of the claimed RMFPNAPYL peptide of SEQ ID NO: 1. The affidavit demonstrates the possession of peptides eluted from antigen presenting cells, but does not disclose the sequence of any of the eluted peptides. It is well known in the art that MHC molecules bind to antigenic peptide fragments not based upon the entire primary sequence of the peptide, but rather on the presence of certain anchor residues within the sequence, with a degree of flexibility regarding the identity of amino acid residues intervening between those anchor residues. Accordingly, the eluates disclosed in the affidavit may represent a single peptide or a mixture of peptides recognized by those antigen-presenting cells and may not include the RMFPNAPYL peptide at all. Therefore, without evidence of the sequence of the peptide eluted from the antigen presenting cells as presented in the affidavit, there is no support of the claimed peptide in the disclosure of antigen presenting cell eluates in the affidavit.

The following represent new grounds of rejection that has not been necessitated by any amendment. Accordingly, this Office Action is made NON-FINAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1, 5, 15 and 19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to any peptide of 9-100 amino acid residues in length comprising the core amino acid sequence RMFPNAPYL (SEQ ID NO: 1), wherein the peptide is processed by HLA-A0201 APCs to produce the peptide of SEQ ID NO: 1. However, the specification teaches only one peptide comprising the RMFPNAPYL amino acid sequence and that is the 9-mer of SEQ ID NO: 1. The specification does not teach any peptides of 10-100 amino acid residues in length that can be processed by APCs to yield the RMFPNAPYL peptide. Applicant has not disclosed whether the HLA-A0201 APCs are professional APCs or non-professional APCs. HLA-A0201 is an MHC class I antigen and is therefore expressed upon all cells in the body, not just on professional APCs. Antigen processing is different between professional APCs and other cells in the body. Professional APCs process antigen in a specialized proteasome called an immunoproteasome. Other types of cells in the body produce antigenic fragments in a standard proteasome. It is known in the art that the antigenic fragments produced by the two types of proteasome are different, due to differences in enzymatic cleavage sites (see e.g., Morel et al. (Immunity [2000] 12:107-117; U on form PTO-892, newly cited). Furthermore, the presence of HLA-A0201 on the surface of the APC does not affect the peptides produced by the APC, only which peptides are presented on the surface of the cell in the context of MHC class I to a corresponding T cell. In other works, a non-HLA-A0201 APC may also produce the antigenic peptide of SEQ ID NO: 1, but that peptide will not be presented upon the surface of the APC to a T cell.

Accordingly, Applicant has not demonstrated the possession of the full genus of 9-100 amino acid residue peptides that can be processed by an HLA-A0201 APC to yield the RMFPNAPYL peptide. Within the genus, Applicant has only demonstrated the possession of the 9-mer peptide of SEQ ID NO: 1. Adequate

written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. See *Fiers v. Revel*, ((CAFC, 1993) 25 USPQ 2d 1601) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, ((CAFC, 1991) 18 USPQ2d 1016).

Vas-Cath Inc. v. Mahurkar ((CAFC, 1991) 19 USPQ2d 1111) clearly states that "Applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See *Vas-Cath* at page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see *Vas-Cath* at page 1115).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1, 5, 7, 15 and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 5 are ambiguous and unclear in the recitation of "HLA-A0201-positive antigen presenting cells." HLA-A is an MHC class I molecule and is therefore present on all cells. it is therefore unclear as to whether the recitation refers to dedicated -or professional- antigen presenting cells, which process antigenic peptides in immunoproteasomes, or non-professional APCs (i.e., any other type of cell), which process antigenic peptides in standard proteasomes. The resultant peptides generated by each type of proteasome are different, resulting in a different pool of antigenic peptides being expressed upon the surface of the cell in context of HLA-A.

Conclusion

4. No claim is allowed.

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to F. Pierre VanderVegt whose telephone number is (571) 272-0852. The examiner can normally be reached on M-Th 6:30-4:00 and Alternate Fridays 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

F. Pierre VanderVegt, Ph.D. FPV
Patent Examiner
August 31, 2005

David A Saunders
DAVID SAUNDERS
PRIMARY EXAMINER
ART UNIT 182 1644